REMARKS/ARGUMENTS

The Status of the Claims.

Claims 1, 11-12, 20-21, 24-26, and 74-75 are pending with entry of this response.

Information Disclosure Statement

Applicants thank the examiner for her consideration of the references submitted in the IDS filed March 15, 2010.

Priority Claims

Benefit of the filing dates of provisional application 60/444,494, filed January 31, 2003, and provisional application 60/519,074, filed November 10, 2003, was denied. As described in detail in the response filed December 10, 2007 and in the response filed August 8, 2008, Applicants have presented a proper priority claim to both documents and respectfully request that priority be acknowledged.

Furthermore, Applicants respectfully request that the refusal to accord priority be reconsidered in light of amendments 5/25/2007 and 12/10/2007. Priority was not accorded because the priority documents were alleged to not correspond to the breadth of the claims. See, Office Action mailed 11/29/2006. Applicants respectfully traverse for reasons of record.

Clarification of previous response.

The Examiner states in the Office Action that Applicants have improperly argued against an anticipation rejection using state of the art arguments. Applicants, to clarify the record, respectfully point out that the state of the art arguments presented were in response to the examiner's use of extrinsic evidence in a rejection under the theory of anticipation by inherency (*see, e.g.*, the Office Action of 11/21/2008), which theory of rejection has apparently been abandoned in favor of the present rejection.

Furthermore, the Examiner alleges that Applicant has not addressed each reference individually. Applicants respectfully point out that each reference cited was addressed individually in the response filed response filed 5/25/2007 and in the response

filed 12/10/2007, which arguments are still maintained by Applicants. In addition, each rejection is individually addressed herein.

The claims are not anticipated under 35 U.S.C. §102.

Claims 1, 11-12, 20-21, 24-26, and 74-75 were rejected under 35 U.S.C. §§102(a) and 102(e) as allegedly anticipated by Timans et al.; under 35 U.S.C. §102(b) as allegedly anticipated by De Sauvage et al. and by Bennet at al.; and under 35 U.S.C. §102(e) as allegedly anticipated by Matthews et al. Applicants respectfully traverse each rejection as provided in the responses filed May 25, 2007, December 10, 2007, August 8, 2008, and August 21, 2009, and March 15, 2010, and for the reasons provided herein.

In order for a reference to anticipate an invention, the reference must teach each and every element of the claimed invention. Anticipation requires that "all limitations of the claim are found in the reference, or 'fully met' by it." Kalman v. Kimberly-Clark Corp., 218 USPQ 781, 789 (Fed. Cir. 1983).

As recently reaffirmed in *Net Moneyin, Inc. v. Verisign, Inc.*, et al. No. 2007-1565, U.S. Court of Appeals for the Federal Circuit, 10/20/2008, to anticipate a claim, the elements of the claim must be in the prior art reference in the same arrangement as in the claim. The Federal Circuit explicitly stated, on page 15, that "Because the hallmark of anticipation is prior invention, the prior art reference—in order to anticipate under 35 U.S.C. § 102—must not only disclose all elements of the claim within the four corners of the document, but must also disclose those elements "arranged as in the claim." *Connell v. Sears, Roebuck & Co.*, 722 F.2d 1542, 1548 (Fed. Cir. 1983)." It further elaborates that "...our precedent informs that the 'arranged as in the claim' requirement applies to all claims and refers to the need for an anticipatory reference to show all of the limitations of the claims arranged or combined in the same way as recited in the claims . . . ."

To anticipate claim 1 and dependents thereto, the prior art must include both of the following steps: (1) a patient having immune hyperactivity must be selected; and (2) that patient must be administered an IL-27R agonist, which agonist is selected from the group consisting of IL-27, an active fragment of IL-27, an agonistic antibody, and a IL-27R binding antibody fragment that enhances IL-27R activity.

For claim 24 and dependents thereto, the prior art must show a patient needing suppression of a T-helper cell mediated immune response, independent of polarization of the immune response, is administered an effective amount of an IL-27R agonist, wherein said agonist is selected from the group consisting of IL-27, an active fragment of IL-27, an agonistic antibody, and a IL-27R binding antibody fragment that enhances IL-27R activity.

Therefore, to support an anticipation rejection over the claimed invention, it is insufficient for a reference to merely disclose all the compositions involved in the claimed methods, e.g., IL-27, IL-27R and antibodies thereto. The reference must also specify the type of condition for which a patient is being treated and with which compounds that patient is treated.

The claims are not anticipated by Timans

Timans is alleged to anticipate the claimed invention by teaching "the administration of IL-27 in the treatment of immune disorders and inflammation (paragraphs 14, 24, 36, 39, 42, 43, 161, and 204; see especially paragraph 39)". See, Office Action, page 4. Paragraph 39 reads as follows:

> "IL-D80 or IL-27 agonists, or antagonists, may also act as functional or receptor antagonists. Thus, IL-D80, IL-27, WSX-1/TCCR, or its antagonists, may be useful in the treatment of abnormal medical conditions, including immune disorders, e.g., T cell immune deficiencies, inflammation, or tissue rejection, or in cardiovascular or neurophysiological conditions."

The first sentence states that agonists and antagonists of ILD80 (also known as p28, one of the subunits of IL-27), and IL-27 can act as functional or receptor antagonists. Applicants are unsure how this applies to the instantly claimed invention as the compound used in the claimed methods is an IL-27R agonist. The next sentence states that IL-27 (a cytokine), ILD80 (a cytokine subunit), WSX-1 (a receptor subunit) and antagonists of WSX-1 can be used in the treatment of abnormal medical conditions, including immune disorders. Various immune disorders are then provided as examples, including both immune deficiencies and inflammation. No data is provided in Timans that could possibly support the idea that all four of these compounds, (p28, IL-27, WSX-1, and WSX-1 antagonists) can or should be used to treat both immune deficiencies and inflammation. Therefore Applicants suggest (1) that this is nothing more than a general paragraph regarding the newly reported

sequences of these compounds and their possible uses; and (2) that to determine what is meant by this paragraph, the entire document must be considered. For example, the section on biological uses might indicate more clearly what Timans teaches about using IL-27 and other WSX-1 agonists.

When one considers the entire Timans reference, the role of IL-27 contemplated by Timans is clearly that of inducing T-cell proliferation, see, e.g., paragraphs 209-211 summarizing the biological effects of IL-27. Paragraph 220 also describes the role of WSX-1 (which is part of the IL-27 receptor) and concludes that WSX-1 is required for IL-27 signal transduction, which signal transduction results in increased T-cell proliferation. Because the data provided in Timans indicate that both WSX-1 and IL-27 are required for increasing T-cell production, it is clear that Timans did not teach or suggest that one should administer a composition comprising IL-27 or a receptor agonist (IL-27R agonist as in claims) to a patient with an inflammatory condition. When read in its entirety, Timans, at most, indicates that the receptor /ligand complex should be used as a drug target for inflammatory conditions because it is involved in inducing inflammation. Timans does not teach using a compound that is a receptor agonist to reduce inflammation.

Therefore, whatever is meant by paragraph 39, Timans does not teach that a person with immune hyperactivity should be selected and administered an IL-27R agonist, e.g., IL-27.

Paragraph 161 (emphasis added) of Timans is also referenced in the Action as support for the anticipation rejection.

> "Taken together the above indicates a role for the composite cytokine and its associated receptor subunit WSX-1/TCCR in inflammatory responses. Therefore **antagonizing the function of any of the components in the receptor subunit:ligand complex should have a beneficial effect in inflammatory diseases,** e.g., inflammatory bowel disease, rheumatoid arthritis, etc."

This paragraph further highlights that Timans, if anything, advocates a role for an **antagonist** of IL-27R in any treatment of an inflammatory response. The claimed methods comprise agonizing the function of one of the components of the receptor subunit/ligand complex to treat an inflammatory or condition. In other words, an **agonist** of IL-27R is used to treat immune hyperactivity. This is not taught in paragraph 39, paragraph 161, or any of the other

cited paragraphs alone or in any combination. Furthermore, when read in its entirety, Timans teaches that an IL-27R antagonist should be given to treat an inflammatory condition.

The claims are not anticipated by De Sauvage

De Sauvage teaches a role for IL-27 in the differentiation of TH1 and TH2 immune responses. Given that De Sauvage teaches that IL-27 would shift an immune response from one type of response to another, it is illogical to suggest that De Sauvage also teaches administration of IL-27, or any other IL-27R agonist, to a person to treat immune hyperactivity.

Pages 59-63 are cited by the office as an alleged teaching that WSX-1 polypeptides and agonist antibodies should be used to treat immune hyperactivity. Applicants respectfully request that the Office be more specific as to where on pages 59-63 this is stated in De Sauvage because Applicants see no such teaching in these pages or anywhere else in the cited document.

Applicants respectfully point out that the claims are drawn to using IL-27 and agonists of WSX-1. A complete reading of pages 59-63 does indeed suggest treatment of many diseases. However, the only compounds mentioned are polypeptides, antibodies and other active compounds. No specific compounds are mentioned. The reference does not state which of the many compounds discussed in the specification should be used for which of the many diseases and conditions. It is illogical to assume that all compounds mentioned in the reference are used for the myriad diseases and conditions listed therein, which list includes both immune deficiency conditions and immune hyperactivity conditions.

De Sauvage may well "contemplate inhibition of molecules with proinflammatory properties" as alleged by the examiner (see, Office Action page 5), but it does not teach how to inhibit proinflammatory molecules in any way, much less teach the presently claimed method. If anything, the reference identifies WSX-1 as a proinflammatory compound, and a WSX-1 agonist as a compound that stimulates or enhances the biological activity of WSX-1 (*see*, page 20), so Applicants question how this could possibly teach one to select a patient with immune hyperactivity and administer a compound, that according to De Sauvage, would enhance the proinflammatory activity of WSX-1.

Pages 8 and 9 of De Sauvage, also cited in Office Action, do nothing more than list various types of immune disorders, including both those that involve immune deficiency and immune hyperactivity. These pages do not contain any reference to how to treat such disorders. It is absurd to suggest that De Sauvage teaches that all types of disorders should be treated with all compounds, e.g., the agonists, antagonists, receptors and cytokines discussed in De Sauvage.

Furthermore, the data presented in Example 12 of De Sauvage teaches agonizing WSX-1 to suppress immune hyperactivity. Example 12 illustrates the role of WSX-1 in immune responses and the role described here is not one that teaches administrating an agonist of WSX-1 to treat immune hyperactivity. In particular Example 12 teaches that WSX-1 deficient mice were unable to mount a Th1 immune response but had an enhanced Th2 response (*see, e.g.*, page 79, lines 16-18). Therefore, antagonizing WSX-1 would lead to decreased Th1 response and increased Th2 response. Presumably, e.g., based on the definition of agonist supplied by De Sauvage, the agonist would do the opposite and provide an enhanced Th1 response and a decreased Th2 response. Based on these teachings, one of skill would not select a person with an immune hyperactivity disorder and administer a WSX-1 agonist to such a patient because it would enhance at least one type of immune response in a person already experiencing hyperactivity of the immune system. There is no logical reason one of skill would, based on De Sauvage, give a patient with immune hyperactivity a compound that increases production of T cells and De Sauvage does not suggest or teach that one should do so.

Page 36 of De Sauvage describes in more detail the role that TCCR (WSX-1) plays in the immune response and exactly what methods are taught by De Sauvage. For example, page 36, lines 7-9 explicitly state that WSX-1 (TCCR) "and its agonists/antagonists may be useful in a therapeutic method to bias the mammalian immune response" towards a Th1 or Th2 response. Because both enhanced production of Th1 or Th2 cells can lead to inflammatory conditions (*see, e.g.*, De Sauvage, page 36, lines 18-25), these compounds are not taught in a method to suppress an immune hyperactivity response as claimed.

Mere mention, in De Sauvage, of the same compounds and types of immune disaseses is insufficient to maintain an anticipation rejection because the compounds and

diseases and methods of treatment, if any, are not arranged in the same manner as the claimed method. The prior art must contain the same elements of the claimed invention in the same combination as the claimed invention. No subject with immune hyperactivity is selected for administration with IL-27 or any other agonist of WSX-1. De Sauvage may mention agonists of WSX-1(TCCR), but it never combines such agonists with a suggestion of treatment for immune hyperactivity.

The examiner has pointed out instances in De Sauvage where broad statements are made that the compounds of the invention are useful in modulating the immune system. However, no specific methods or combinations of compounds and direction of modulation are provided by these statements. Upon closer inspection, e.g., Example 12, it is clear that the reference teaches that TCCR (WSX-1) is a stimulator of T cell production. On page 40 of De Sauvage, line 33-36, it specifically states that "polypeptides of the invention . . . which are stimulators (costimulators) of T cell proliferation and agonists , e.g., agonists antibodies, thereto . . . are useful in treating immune related diseases characterized by poor, suboptimal or inadequate immune function." Therefore, De Sauvage does not teach administering an agonist of WSX-1 to a patient with immune hyperactivity.

While agonist antibodies of IL-27R may be discussed in De Sauvage, the only use for such agonists taught by De Sauvage is in the differentiation of helper T cells. De Sauvage teaches that agonists and antagonists of IL-27R shift the balance between Th1 and Th2 type immune responses. This does not provide immune suppression as claimed, merely polarization of the immune response. An agonist or antagonist is not administered in De Sauvage to suppress the immune system; they administer the agonist/antagonist to switch the type of immune response a patient experiences. Therefore, De Sauvage does not teach every element of the claimed invention in the claimed configuration.

The claims are not anticipated by Bennett

The Office Action alleges that Bennett teaches methods of using WSX-1 ligands and agonist antibodies (Office Action pages 5-6). However, the methods it teaches are not the same as the claimed methods of using agonist antibodies to WSX-1. For example, the office refers to pages 4 and 5. After careful review, Applicants note that page 4, lines 19-

20 states that agonist ligands or antibodies of WSX-1 "may be used to stimulate proliferation of stem cells . . . ." Page 5, lines 12-13, states that the agonist antibody may "induce lymphopoiesis, erythropoiesis and/or myelopoiesis." Applicants are unclear how this can be construed as a method comprising (1) selecting a patient with immune hyperactivity and (2) administering an IL27R agonist to the patient. If Bennett teaches using the agonist antibodies of WSX-1 to induce the formation of lymphocytes, bone marrow cells, or blood cells, how does Bennett teach the claimed method, of giving those same compounds to a patient who is experiencing immune hyperactivity. Bennett does not teach or even vaguely suggest that a subject with immune hyperactivity be given these compounds.

Page 6 of Bennett is also referenced in the Office Action. Upon review of page 6, Applicants note that lines 21-23 state that WSX-1 receptor "antagonists . . . may be used in the treatment of those disorders wherein unacceptable lymphocyte levels are present in the mammal," and specifies that antagonists can be used to treat lymphoma and leukemia" This does not teach the claim elements in the same arrangement as the claimed method.

Page 41, also cited by the examiner, describes therapeutic uses for the WSX-1 receptor itself, not the compounds used in the claimed methods, i.e., IL-27, an active fragment of IL-27, an agonistic antibody to IL-27R, or an IL-27R binding antibody fragment.

Pages 56-59 of Bennett are also cited in the Office Action, but they too indicate that an agonist antibody should be used to enhance proliferation of hematopoieitc cells, lines 28-26-28. Although there may exist some overlap between the disorders and conditions listed in claim 21 with the disorders listed in various parts of Bennett (as well as other cited art), Applicants respectfully point out that claim 21 is dependent from claim 1, which includes the limitation that the patient, to whom the IL-27R agonist is administered, have immune hyperactivity. At no point does Bennett teach that a person with immune hyperactivity be administered an agonist of IL-27R or WSX-1.

The claims are not anticipated by Matthews

Matthews discusses WSX-1 as a target to affect hematopoietic stem cells, which are blood forming stem cells in the bone marrow from which cells T cells and B cells arise. Although Matthews contains the words "agonist" and "antibody" and "WSX-1" and

"treatment" and perhaps mentions of some of the same diseases that are included in the claimed method, these words are not arranged in a manner that anticipates the claimed methods. In other words, Matthews specifically states in column 3, lines 58-61, (the same paragraph to which the Office action refers for a reference to agonist antibodies to WSX-1), that potential patients include those who have undergone chemo- or radiation therapy or bone marrow transplantation therapy. This is not the patient population selected in the claimed method. It is Applicants' understanding that patients who have undergone chemo- or radiation therapy or bone marrow transplantation therapy do not typically have immune hyperactivity and/or need immune suppression. Matthews may teach what an agonist antibody to WSX-1 does, e.g., stimulate theWSX-1 receptor, but it does not teach or suggest that a patient with immune hyperactivity needs to have WSX-1 stimulated or that such a patient be given a WSX-1 agonist. In fact, it explicitly states the opposite, that those in need of immune system stimulation be given these agonist antibodies, e.g., those in need of WSX-1 receptor activation. *See, e.g.*, column 17, lines 15-16, indicating that agonist antibodies to WSX-1 be used to stimulate proliferation of hematopoietic stem cells.

Applicants respectfully request that the Examiner more specifically point out where the idea of an agonist antibody of WSX-1 or IL27R is mentioned specifically in connection with treating immune hyperactivity. Applicants see that the references discuss antibodies, and agonist antibodies and various immune disorders but the cited reference must teach all elements of the claimed method in the same arrangement as the claimed method and pointing out where all the various words of the claim can be found in the reference is not the same as pointing out where they are arranged in the same manner as that claimed.

The rejection under 35 U.S.C. § 102 cannot be maintained.

"Because the hallmark of anticipation is prior invention, the prior art reference—in order to anticipate under 35 U.S.C. § 102—must not only disclose all elements of the claim within the four corners of the document, but must also disclose those elements "arranged as in the claim." *Connell v. Sears, Roebuck & Co.*, 722 F.2d 1542, 1548 (Fed. Cir. 1983). To maintain the above rejections, the Office must show exactly where the specific method of selecting a person with immune hyperactivity for administration of a WSX-1

agonist (Claim 1) or a patient in need of immune suppression (independent of polarization of the immune response) of a T-helper cell mediated immune response, is administered an effective amount of an IL-27R agonist, wherein said agonist is selected from the group consisting of IL-27, an active fragment of IL-27, an agonistic antibody, and a IL-27R binding antibody fragment (Claim 24).

For all references on which the 35 U.S.C. § 102 rejection is based, the Office has shown no more than that many elements of the claimed method are disclosed in the four corners of the documents. The Office has not shown where the references cited disclose those elements arranged as in the claim. The office has merely provided a disjointed list of where each of the words in the claim can be found in the cited art. This is insufficient to uphold a rejection for anticipation. Therefore, Applicants respectfully request that the rejections be withdrawn.

Non-Statutory Obvious-Type Double Patenting

Claims 1, 6, 11-13, 18-23, and 73 were provisionally rejected for alleged non-statutory obvious-type double patenting over claims 21-24 and 26-28 of co-pending application 11/880,121. The Examiner requested that a terminal disclaimer be filed under 37 C.F.R. § 1.321(c) or (d). When all substantive issues have been resolved and the claims are otherwise in condition for allowance, Applicants will submit a terminal disclaimer over the claims of USSN 11/880,121 if it is still necessary at that time.

CONCLUSION

In view of the foregoing, Applicants believes all claims now pending in this application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

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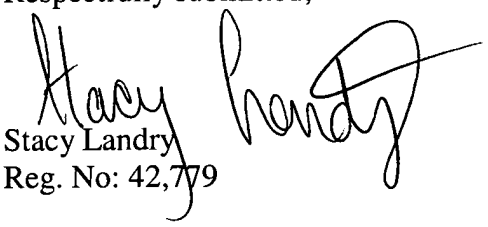

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